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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/502,235	07/22/2004	Malgorzata Anna Kisielow	I-32330A/FMI	9191
1095 NOVARTIS CORPORATE INTELLECTUAL PROPERTY ONE HEALTH PLAZA 104/3 EAST HANOVER, NJ 07936-1080	7590 03/07/2007		EXAMINER SAJJADI, FEREYDOUN GHOTB	
			ART UNIT 1633	PAPER NUMBER PAPER
			MAIL DATE 03/07/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Advisory Action Before the Filing of an Appeal Brief</b>	Application No.	Applicant(s)
	10/502,235	KISIELOW ET AL.
	Examiner Fereydoun G. Sajjadi	Art Unit 1633

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 12 February 2007 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1.  The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a)  The period for reply expires 6 months from the mailing date of the final rejection.
- b)  The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### NOTICE OF APPEAL

2.  The Notice of Appeal was filed on 2/12/2007. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

#### AMENDMENTS

- 3.  The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
  - (a)  They raise new issues that would require further consideration and/or search (see NOTE below);
  - (b)  They raise the issue of new matter (see NOTE below);
  - (c)  They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
  - (d)  They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_. (See 37 CFR 1.116 and 41.33(a)).

- 4.  The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
- 5.  Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.
- 6.  Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

7.  For purposes of appeal, the proposed amendment(s): a)  will not be entered, or b)  will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: \_\_\_\_\_.

Claim(s) objected to: \_\_\_\_\_.

Claim(s) rejected: 1-12 and 14-20.

Claim(s) withdrawn from consideration: 13 and 21-23.

#### AFFIDAVIT OR OTHER EVIDENCE

- 8.  The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
- 9.  The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).

10.  The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

#### REQUEST FOR RECONSIDERATION/OTHER

- 11.  The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Attachment to Advisory.
- 12.  Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). \_\_\_\_\_
- 13.  Other: \_\_\_\_\_

Continuation of 11: The rejection of claims 1-12 and 14-20 under 35 USC 112, first paragraph, as lacking written description support is maintained for reasons of record. Applicants disagree with the rejection, arguing that there is no substantial variation within the genus of all gene products that are alternatively spliced to generate specific isoforms, because the gene products themselves are not essential to the claimed invention and their functional, biological or structural properties do not at all impact the property of the claimed methods. Applicants arguments have been fully considered, but are not found persuasive.

It is maintained that detailed structural knowledge of any alternatively spliced gene products is a requisite for producing an siRNA double stranded nucleic acid having at least 95% sequence identity to a common nucleic acid shared by two or more isoforms of said gene products and further producing a specific isoform having one or more mismatches relative to said double stranded portion of said nucleic acid. As previously indicated, an RNA interference ds ribonucleic acid must be designed in a sequence specific manner to form a specific secondary structure, requiring knowledge of the structure and sequences of the spliced variants of a target gene product, and further, empirically tested to ascertain proper suppression of expression of all the isoforms in the cell.

In response to Applicants' argument that a practitioner of the present method claims only need possess knowledge relating to her gene product of interest, it is maintained that possession for the gene product of interest of the instant invention (i.e. the Shc gene family) has been indicated. However, the instant claims read on any gene isoform, including those yet to be discovered. In response to Applicants' argument that there is no requirement to explicitly list every isoform for a gene product of interest in the specification as they are inherent in the present invention, it is maintained that the detailed structure and sequences provided for the Shc gene family is insufficient to demonstrate possession for any of the enormous number of alternatively spliced gene products that differ in sequence structure and function from that of the Shc gene.

The rejection of claims 1-12 and 14-20 under 35 USC 112, first paragraph, as lacking an enablement for the full scope of the claimed invention, is maintained for reasons of record. Applicants disagree with the rejection, arguing that the claim amendments to include only in vitro methods obviate the major aspects of the enablement rejection. While the limitations

introduced into the instant claims in part address the issues regarding the enablement rejection, additional issues regarding the unpredictability of attenuating expression of numerous target genes by RNAi in different cell types for which adequate structural details need to be determined, remain and would require further undue experimentation.

The rejection of claims 1-12 and 14-20 under 35 USC 102(e), as anticipated by Tuschl et al. is maintained because the effective 102(e) date of the reference is the filing date of its related U.S. provisional application 60/279,661 (i.e. Mar. 30, 2001. Thus, the 37CFR 1.131 declaration by inventor Kisielow is insufficient to overcome the rejection. The claim rejections are thus maintained for reasons of record and the foregoing discussion.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fereydoun G. Sajjadi whose telephone number is (571) 272-3311. The examiner can normally be reached Monday through Friday, between 7:00 am-4:00 pm EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free). Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Fereydoun G. Sajjadi, Ph.D.  
Examiner, Art Unit 1633

  
ANNE M. WEMBE, PH.D.  
PRIMARY EXAMINER

